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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/003,669	11/01/2001	Robert H. Broyles	649.001	5327

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EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1633	

MAIL DATE	DELIVERY MODE
05/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/003,669	BROYLES ET AL.	
	Examiner	Art Unit	
	Q. JANICE LI	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-31,35,37 and 38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-31,35,37 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment and response filed 3/17/08 are acknowledged. Claims 32-34, 36 have been canceled. Claims 37, 38 are newly submitted. Claims 29-31, 35, 37, 38 are pending and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in 3/17/08 response would be addressed to the extent that they apply to current rejection.

Interview Summary

A telephonic interview was conducted in the attendances of Supervisor Examiner Joseph Woitach, the applicant's representative Barbara Yuill, and the inventor Robert Broyles.

The applicant presented the reasoning for the amendment of claims, and arguments particularly concerning how the amended claims would distinguish from the art rejection (Picard et al). The examiners presented the Office position with regard to the applicant's argument, which will be reflected in the new rejections and Response to Argument below.

Possible approaches to overcome the rejection of record were also discussed.

New grounds of rejections are necessitated in view of claim amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The prior rejection of Claims 29-31, 35, 37, 38 stand or newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, for reasons of record and following.

Although the amended claims do not recite a method for treating sickle cell disease, given the broadest reasonable interpretation in light of the specification, instant claims implicitly encompass the embodiment of treating a sickle cell disease, particularly in view of the claim language encompasses a process *in vivo*. Further in light of the specification, the real world utility for repressing production of beta-globin in a cell is for therapeutic purpose for treating sickle cell diseases.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The prior rejection of Claims 29-31, 33-36 under 35 U.S.C. 102(b) as being anticipated by *Picard et al* (Blood 1996;87:2057-64, IDS), is withdrawn in view of claim amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 29-31, 35, 37, 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Picard et al* (Blood 1996;87:2057-64, IDS).

Claims as written encompass an embodiment wherein the nucleic acids transfect globin-producing cell *in vitro*.

Picard et al teach a method comprising the step of providing a vector encoding ferritin-H (e.g. fig. 1), and inserting the vector into beta-globin producing cell MEL, whereby ferritin-H is produced in the cell (e.g. fig. 2), which would lead to repression of beta-globin proteins in the cell. *Picard et al* teach heme synthesis is reduced in cells overexpressing the H-ferritin (column 2, page 2060). *Picard et al* stated "A REDUCED ACCUMULATION OF β-GLOBIN MRNA WAS ALSO OBSERVED, WHICH COULD ACCOUNT FOR THE IMPAIRED HEMOGLOBIN SYNTHESIS" (see e.g. the abstract), and "THE RESULTS IN FIG 5 PATENTLY REVEAL AN OVERALL REDUCTION IN THE AMOUNT OF HEMOGLOBIN THAT ACCUMULATES IN THE VARIOUS CLONES TESTED, IN INVERSE RELATIONSHIP WITH THE AMOUNT OF H-MRNA FROM THE TRANSFECTED GENE" (column 2, page 2060). Apparently, *Picard et al* were fully aware the repression of β-globin mRNA, and its effect on the production of β-globin because of the well known association between levels of mRNA and that of the protein and because

they observed impaired production of hemoglobin protein synthesis, for which β-globin is a subunit component. Hence, even though *Picard et al* do not explicitly teach or prove that β-globin was repressed, viewing the data presented, it would have been reasonably suggested to the skilled in the art that β-globin protein production would be repressed.

Picard et al differ from instant claims in that they used mouse cells and mouse Ferritin-H for the vector construct, not humans. However, it was well known in the art the ultimate goal of animal studies was for treating diseases in humans, and hence it would have suggested to the skilled in the art to further the studies in human cells using human ferritin-H. In fact, *Picard et al* clearly stated, "A FERRITIN-LIKE PROTEIN HAS BEEN FOUND IN NUCLEAR EXTRACTS OF K562 CELLS, AND THERE IS SOME EVIDENCE THAT IT CAN ACT AS A REPRESSOR OF ADULT B-GLOBIN GENE EXPRESSION. THIS WOULD BE CONSISTENT WITH THE REDUCED B-GLOBIN MRNA ACCUMULATION IN OUR TRANSFECTED CLONES" (column 2, page 2063), which implicitly suggested the connection between the mouse and human (K562 cells are human β-globin producing cells), and provided reasonable expectation of success when applying the method in mouse cells to human cells. Accordingly, the claimed invention as a whole was prima facie obvious in the absence of evidence to the contrary.

Response to Arguments

In the response, the applicant first argues that Picard et al. do not teach or disclose the binding of ferritin-H to the promoter region of the beta-globin gene nor effect of this binding, and pointing to Pountney as support of the argument.

The argument has been fully considered but found not persuasive because the binding of ferritin-H to the promoter region is the underlying mechanism concerning how ferritin-H asserts its effect upon administering the vector to the cell, which is a necessary consequence of the administration. Accordingly, even though *Picard et al* or *Pountney et al* did not recognize the mechanism of ferritin-H action as claimed by the applicant, they fully disclose the instantly claimed method steps and the effects on production. Applicant is reminded that it is a general rule that merely discovering and claiming a new benefit to an old process cannot render the process again patentable. *In re Woodruff* 919 F. 2d 1575, 1577-78, 16 USPQ2d 1934, 1936-37 (Fed. Cir. 1990); *In re Swinehart*, 439 F. 2d 210, 213, 169 USPQ 226, 229 (CCPA 1971); and *Ex Parte Novitski*, 26 USPQ2d 1389, 1391 (Bd. Pat. App. & Int. 1993).

The applicant then argues that the vector used by *Picard et al* overexpresses a mutated mouse H-ferritin gene.

In response, it is noted the mutation occurs in the 5' untranslated region affecting iron responsive element of the H-ferritin gene but it did not affect the integrity of the ferritin-H protein itself.

The applicant went on to argue that a statement concerning a general reduction of heme synthesis does not distinguish between alpha-, beta- and gamma-globins, and thus a reduction in heme synthesis does not support a reduction in synthesis of a specific globin, and teaches away from an increase in gamma-globin.

In response, when *Picard et al* disclosed the reduction of β-globin mRNA, it reasonably suggested to the skilled in the art the decrease of the β-globin protein

production. As to the gamma-globins, again, it is the necessary consequence of administering H-ferritin expression vector.

The applicant then points to the communication from European patent office.

In response, the applicant is reminded each application is examined on its own merits and cannot be compared to other application. Even for applications in the U.S. patent system, the court (*In re Giolito and Hofmann*, 188 USPQ 645 (CCPA 1976)) states "IT IS IMMATERIAL WHETHER SIMILAR CLAIMS HAVE BEEN ALLOWED TO OTHERS. SEE IN RE MARGAROLI, 50 CCPA 1400, 318 F.2D 348, 138 USPQ 158 (163); IN RE WRIGHT, 45 CCPA 1005, 256 F.2D 583, 118 USPQ 287 (158); IN RE LAUNDER, 41 CCPA 887, 212 F.2D 603, 101 USPQ 391 (1954)." As to the specific globins affected by the H-ferritin, the argument has been addressed *supra*.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on 571-272-0739. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

For all other customer support, please call the USPTO Call Center (UCC) at **800-786-9199**.

/Q. JANICE LI/
Primary Examiner, Art Unit 1633

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QJL

May 18, 2008